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FILE LAST UPDATED: 16 Nov 2005 (20051116/ED)

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=> HEK293

L1 2736 HEK293

=> reovirus

1967 REOVIRUS

332 REOVIRUSES

L2 2036 REOVIRUS

(REOVIRUS OR REOVIRUSES)

=> reassorted

L3 49 REASSORTED

=> L2 and L3

L4 1 L2 AND L3

=> L1 and L4

L5 0 L1 AND L4

=> L1 and L2

L6 5 L1 AND L2

=> D L5 IBIB ABS 1-5

L5 HAS NO ANSWERS

L1 2736 SEA FILE=CAPLUS ABB=ON PLU=ON HEK293

L2 2036 SEA FILE=CAPLUS ABB=ON PLU=ON REOVIRUS

L3 49 SEA FILE=CAPLUS ABB=ON PLU=ON REASSORTED

L4 1 SEA FILE=CAPLUS ABB=ON PLU=ON L2 AND L3

L5 0 SEA FILE=CAPLUS ABB=ON PLU=ON L1 AND L4

=> D L6 IBIB ABS1-5

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L6 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2005:439832 CAPLUS  
DOCUMENT NUMBER: 143:227017  
TITLE: Inhibition of NF- $\kappa$ B activity and cFLIP  
expression contribute to viral-induced apoptosis  
AUTHOR(S): Clarke, P.; DeBiasi, R. L.; Meintzer, S. M.; Robinson,  
B. A.; Tyler, K. L.  
CORPORATE SOURCE: Departments of Neurology, University of Colorado  
Health Sciences Center, Denver, CO, 80262, USA  
SOURCE: Apoptosis (2005), 10(3), 513-524  
CODEN: APOPFN; ISSN: 1360-8185  
PUBLISHER: Springer  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS  
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=> D L6 IBIB abs 1-5

L6 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN  
ACCESSION NUMBER: 2005:439832 CAPLUS  
DOCUMENT NUMBER: 143:227017  
TITLE: Inhibition of NF- $\kappa$ B activity and cFLIP

AUTHOR(S): expression contribute to viral-induced apoptosis  
 Clarke, P.; DeBiasi, R. L.; Meintzer, S. M.; Robinson,  
 B. A.; Tyler, K. L.  
 CORPORATE SOURCE: Departments of Neurology, University of Colorado  
 Health Sciences Center, Denver, CO, 80262, USA  
 SOURCE: Apoptosis (2005), 10(3), 513-524  
 CODEN: APOPFN; ISSN: 1360-8185  
 PUBLISHER: Springer  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Virus-induced activation of nuclear factor-kappa B (NF- $\kappa$ B) is  
 required for Type 3 (T3) **reovirus**-induced apoptosis. We now  
 show that NF- $\kappa$ B is also activated by the prototypic Type 1  
**reovirus** strain Lang (T1L), which induces significantly less  
 apoptosis than T3 viruses, indicating that NF- $\kappa$ B activation alone is  
 not sufficient for apoptosis in **reovirus**-infected cells. A  
 second phase of virus-induced NF- $\kappa$ B regulation, where NF- $\kappa$ B  
 activation is inhibited at later times following infection with T3 Abney  
 (T3A), is absent in T1L-infected cells. This suggests that inhibition of  
 NF- $\kappa$ B activation at later times post infection also contributes to  
**reovirus**-induced apoptosis. **Reovirus**-induced inhibition  
 of stimulus-induced activation of NF- $\kappa$ B is significantly associated  
 with apoptosis following infection of **HEK293** cells with  
 reassortant **reoviruses** and is determined by the T3 S1 gene segment,  
 which is also the primary determinant of **reovirus**-induced  
 apoptosis. Inhibition of stimulus-induced activation of NF- $\kappa$ B also  
 occurs following infection of primary cardiac myocytes with apoptotic (8B)  
 but not non-apoptotic (T1L) **reoviruses**. Expression levels of  
 the NF- $\kappa$ B-regulated cellular FLICE inhibitory protein (cFLIP)  
 reflect NF- $\kappa$ B activation in **reovirus**-infected cells.  
 Further, inhibition of NF- $\kappa$ B activity and cFLIP expression promote  
 T1L-induced apoptosis. These results demonstrate that inhibition of  
 stimulus-induced activation of NF- $\kappa$ B and the resulting decrease in  
 cFLIP expression promote **reovirus**-induced apoptosis.

REFERENCE COUNT: 75 THERE ARE 75 CITED REFERENCES AVAILABLE FOR THIS  
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L6 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:697089 CAPLUS  
 DOCUMENT NUMBER: 139:207772

TITLE: The use of ribozymes in the detection of adventitious  
 agents for **reovirus** preparation useful in  
 cancer therapy

INVENTOR(S): Coffey, Matthew C.  
 PATENT ASSIGNEE(S): Oncolytics Biotech Inc., Can.  
 SOURCE: PCT Int. Appl., 26 pp.  
 CODEN: PIXXD2

DOCUMENT TYPE: Patent  
 LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003072811	A2	20030904	WO 2003-CA264	20030226
WO 2003072811	A3	20040205		
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW			
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CA 2374388	AA	20030828	CA 2002-2374388	20020304
CA 2374388	C	20030828		
US 2004005546	A1	20040108	US 2003-375700	20030226

EP 1481084	A2	20041201	EP 2003-704136	20030226
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
BR 2003007882	A	20041228	BR 2003-7882	20030226
TR 200501513	T3	20050621	TR 2005-200501513	20030226
JP 2005518797	T2	20050630	JP 2003-571491	20030226
PRIORITY APPLN. INFO.:			US 2002-360730P	P 20020228
			US 2003-441760P	P 20030123
			WO 2003-CA264	W 20030226

AB The present invention provides a method of detecting adventitious agents in a composition comprising a microorganism by using ribozyme-expressing indicator cells, as well as indicator cells useful in such detection. The method is used to ensure that the **reovirus** preparation, used for tumor therapy, does not contain adventitious agents, which may result in undesired side effects. In particular, also disclosed is a method of preparing **reovirus** using mammalian cells (such as **HEK293** or COS-1) stably transfected with ribozyme, Rz-538 or Rz-984, which cleaves **reovirus** genome in case of the presence of adventitious agents.

L6 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2003:366194 CAPLUS

DOCUMENT NUMBER: 139:20428

TITLE: Two Distinct Phases of Virus-induced Nuclear Factor  $\kappa$ B Regulation Enhance Tumor Necrosis Factor-related Apoptosis-inducing Ligand-mediated Apoptosis in Virus-infected Cells

AUTHOR(S): Clarke, Penny; Meintzer, Suzanne M.; Moffitt, Lisa A.; Tyler, Kenneth L.

CORPORATE SOURCE: Departments of Neurology, University of Colorado Health Science Center, Denver, CO, 80220, USA

SOURCE: Journal of Biological Chemistry (2003), 278(20), 18092-18100

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Cellular transcription factors are often utilized by infecting viruses to promote viral growth and influence cell fate. The authors have previously shown that nuclear factor  $\kappa$ B (NF- $\kappa$ B) is activated after **reovirus** infection and that this activation is required for virus-induced apoptosis. In this report the authors identify a second phase of **reovirus**-induced NF- $\kappa$ B regulation. The authors show that at later times post-infection NF- $\kappa$ B activation is blocked in **reovirus**-infected cells. This results in the termination of virus-induced NF- $\kappa$ B activity and the inhibition of tumor necrosis factor  $\alpha$  and etoposide-induced NF- $\kappa$ B activation in infected cells. **Reovirus**-induced inhibition of NF- $\kappa$ B activation occurs by a mechanism that prevents I $\kappa$ B $\alpha$  degradation and that is blocked in the presence of the viral RNA synthesis inhibitor, ribavirin. **Reovirus**-induced apoptosis is mediated by tumor necrosis factor-related apoptosis inducing ligand (TRAIL) in a variety of epithelial cell lines. Herein the authors show that ribavirin inhibits **reovirus**-induced apoptosis in TRAIL-resistant **HEK293** cells and prevents the ability of **reovirus** infection to sensitize TRAIL-resistant cells to TRAIL-induced apoptosis. Furthermore, TRAIL-induced apoptosis is enhanced in **HEK293** cells expressing I $\kappa$ BAN2, which blocks NF- $\kappa$ B activation. These results indicate that the ability of **reovirus** to inhibit NF- $\kappa$ B activation sensitizes **HEK293** cells to TRAIL and facilitates virus-induced apoptosis in TRAIL-resistant cells. These findings demonstrate that two distinct phases of virus-induced NF- $\kappa$ B regulation are required to efficiently activate host cell apoptotic responses to **reovirus** infection.

REFERENCE COUNT: 62 THERE ARE 62 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:607491 CAPLUS  
DOCUMENT NUMBER: 138:54436  
TITLE: **Reovirus**-induced apoptosis requires both death receptor- and mitochondrial-mediated caspase-dependent pathways of cell death  
AUTHOR(S): Kominsky, D. J.; Bickel, R. J.; Tyler, K. L.  
CORPORATE SOURCE: Department of Neurology, University of Colorado Health Science Center, Denver, CO, 80262, USA  
SOURCE: Cell Death and Differentiation (2002), 9(9), 926-933  
CODEN: CDDIEK; ISSN: 1350-9047  
PUBLISHER: Nature Publishing Group  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Apoptosis plays an important role in the pathogenesis of many viral infections. Despite this fact, the apoptotic pathways triggered during viral infections are incompletely understood. The authors now provide the first detailed characterization of the pattern of caspase activation following infection with a cytoplasmically replicating RNA virus. **Reovirus** infection of **HEK293** cells results in the activation of caspase-8 followed by cleavage of the pro-apoptotic protein Bid. This initiates the activation of the mitochondrial apoptotic pathway leading to release of cytochrome c and activation of caspase-9. Combined activation of death receptor and mitochondrial pathways results in downstream activation of effector caspases including caspase-3 and caspase-7 and cleavage of cellular substrates including PARP. Apoptosis is initiated by death receptor pathways but requires mitochondrial amplification producing a biphasic pattern of caspase-8, Bid, and caspase-3 activation.

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2002:209874 CAPLUS  
DOCUMENT NUMBER: 136:382804  
TITLE: **Reovirus**-induced alterations in gene expression related to cell cycle regulation  
AUTHOR(S): Poggioli, George J.; DeBiasi, Roberta L.; Bickel, Ryan; Jotte, Robert; Spalding, Aaron; Johnson, Gary L.; Tyler, Kenneth L.  
CORPORATE SOURCE: Department of Microbiology, University of Colorado Health Sciences Center, Denver, CO, 80220, USA  
SOURCE: Journal of Virology (2002), 76(6), 2585-2594  
CODEN: JOVIAM; ISSN: 0022-538X  
PUBLISHER: American Society for Microbiology  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Mammalian **reovirus** infection results in perturbation of host cell cycle progression. Since **reovirus** infection is known to activate cellular transcription factors, we investigated alterations in cell cycle-related gene expression following **HEK293** cell infection by using the Affymetrix U95A microarray. Serotype 3 **reovirus** infection results in differential expression of 10 genes classified as encoding proteins that function at the G1-to-S transition, 11 genes classified as encoding proteins that function at G2-to-M transition, and 4 genes classified as encoding proteins that function at the mitotic spindle checkpoint. Serotype 1 **reovirus** infection results in differential expression of four genes classified as encoding proteins that function at the G1-to-S transition and three genes classified as encoding proteins that function at G2-to-M transition but does not alter any genes classified as encoding proteins that function at the mitotic spindle checkpoint. We have previously shown that serotype 3, but not serotype 1, **reovirus** infection induces a G2-to-M transition arrest resulting from an inhibition of cdc2 kinase activity. Of the differentially expressed genes encoding proteins regulating the G2-to-M transition, chk1, weel, and GADD45 are known to inhibit cdc2 kinase activity. A hypothetical model describing serotype 3 **reovirus**-induced inhibition of cdc2 kinase is presented, and **reovirus**-induced perturbations of the G1-to-S, G2-to-M, and mitotic spindle checkpoints are discussed.

REFERENCE COUNT:

87

THERE ARE 87 CITED REFERENCES AVAILABLE FOR THIS  
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<u>L11</u>	L9 and L5L10	0	<u>L11</u>
<u>L10</u>	L9 and L5L9	0	<u>L10</u>
<u>L9</u>	HEK and 293	5699	<u>L9</u>
<u>L8</u>	L5 and HEK293	0	<u>L8</u>
<u>L7</u>	L6 and reassorted	0	<u>L7</u>
<u>L6</u>	L5 and reovirus	16	<u>L6</u>
<u>L5</u>	Coffey M.in.	69	<u>L5</u>
<u>L4</u>	L3 and HEK293	0	<u>L4</u>
<u>L3</u>	reassorted adj reovirus	5	<u>L3</u>
<u>L2</u>	assorted adj reovirus	0	<u>L2</u>
<u>L1</u>	assorted adj revirus	0	<u>L1</u>

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